

ABSTRACT

Amphipathic lytic peptides are ideally suited to use in a ligand/cytotoxin combination to specifically inhibit cells that are driven by or are dependent upon a specific ligand interaction; for example, to induce sterility or long-term contraception, or to attack tumor cells, or to selectively lyse virally-infected cells, or to attack lymphocytes responsible for autoimmune diseases. The peptides act directly on cell membranes, and need not be internalized. Administering a combination of gonadotropin-releasing hormone (GnRH) (or a GnRH agonist) and a membrane-active lytic peptide produces long-term contraception or sterilization in animals *in vivo*. Administering *in vivo* a combination of a ligand and a membrane-active lytic peptide kills cells with a receptor for the ligand. The compounds are relatively small, and are not antigenic. Lysis of gonadotropes has been observed to be very rapid (on the order of ten minutes.) Lysis of tumor cells is rapid. The two components -- the ligand and the lytic peptide -- may optionally be administered as a fusion peptide, or they may be administered separately, with the ligand administered slightly before the lytic peptide, to activate cells with receptors for the ligand, and thereby make those cells susceptible to lysis by the lytic peptide. The compounds may be used in gene therapy to treat malignant or non-malignant tumors, and other diseases caused by clones or populations of "normal" host cells bearing specific receptors (such as lymphocytes), because genes encoding a lytic peptide or encoding a lytic peptide/peptide hormone fusion may readily be inserted into hematopoietic stem cells or myeloid precursor cells.